

# CLAIMS

We claim:

- 1 1. A method for early detection of subacute, potentially catastrophic infectious  
2 illness in a premature newborn infant comprising:  
3 (a) continuously monitoring heart rate variability in the premature newborn infant;  
4 and  
5 (b) identifying at least one characteristic abnormality in the heart rate variability that  
6 is associated with the illness.
- 1 2. The method of claim 1, wherein the illness is sepsis.
- 1 3. The method of claim 2, wherein antibiotic therapy is initiated and a diagnostic  
2 work-up for the illness, comprising obtaining a blood culture from the newborn  
3 infant, is provided when the at least one characteristic abnormality is identified.
- 1 4. The method of claim 1, wherein the illness is necrotizing enterocolitis.
- 1 5. The method of claim 4, wherein a diagnostic work-up for the illness, comprising  
2 an X-ray of the newborn infant or a pathological specimen from the newborn infant,  
3 is provided when the at least one characteristic abnormality is identified.
- 1 6. The method of claim 1, wherein the illness is selected from the group consisting  
2 of pneumonia and meningitis.
- 1 7. The method of claim 1, wherein the at least one characteristic abnormality is  
2 identified from a normalized data set of RR intervals.
- 1 8. The method of claim 7, wherein the data set contains on the order of about  $10^3$  to  
2  $10^4$  sequential RR intervals.

- 1 9. The method of claim 7, wherein the at least one characteristic abnormality is  
2 identified based on at least one of the third and higher moments of the data set.
- 1 10. The method of claim 9, wherein the at least one moment of the data set includes  
2 the skewness of the data set.
- 1 11. The method of claim 10, wherein the illness is selected from the group  
2 consisting of sepsis and necrotizing enterocolitis.
- 1 12. The method of claim 9, wherein the wherein the at least one moment of the data  
2 set includes the kurtosis of the data set.
- 1 13. The method of claim 12, wherein the illness is selected from the group  
2 consisting of sepsis and necrotizing enterocolitis.
- 1 14. The method of claim 7, wherein the at least one characteristic abnormality is  
2 identified based on at least one percentile value of the data set.
- 1 15. The method of claim 14, wherein the at least one percentile value is the 10th  
2 percentile value.
- 1 16. The method of claim 15, wherein the illness is selected from the group  
2 consisting of sepsis and necrotizing enterocolitis.
- 1 17. The method of claim 7, wherein the at least one characteristic abnormality is  
2 identified based on the variance, standard deviation or coefficient of variation of the  
3 data set.
- 1 18. The method of claim 17, wherein the illness is selected from the group  
2 consisting of sepsis and necrotizing enterocolitis.

- 1 19. The method of claim 10, further comprising a diagnostic work-up.
- 1 20. The method of claim 12, further comprising a diagnostic work-up.
- 1 21. The method of claim 15, further comprising a diagnostic work-up.
- 1 22. The method of claim 17, further comprising a diagnostic work-up.
- 1 23. The method of claim 1, wherein a diagnostic work-up is provided when the at  
2 least one characteristic abnormality is identified.
- 1 24. A method for early detection of subacute, potentially catastrophic infectious  
2 illness in a patient comprising:  
3 (a) continuously monitoring the patient's RR intervals;  
4 (b) generating a normalized data set of the RR intervals;  
5 (c) calculating one or more of (i) moments of the data set selected from the third and  
6 higher moments and (ii) percentile values of the data set; and  
7 (d) identifying an abnormal heart rate variability associated with the illness based on  
8 one or more of the moments and the percentile values.
- 1 25. The method of claim 24, wherein the moments include the third moment of the  
2 data set.
- 1 26. The method of claim 24, wherein the moments include the fourth moment of the  
2 data set.
- 1 27. The method of claim 24, wherein the percentile values include the 10th  
2 percentile value.
- 1 28. An apparatus for early detection of subacute, potentially catastrophic infectious  
2 illness in a premature newborn infant comprising:

- 3 (a) a monitoring device, continuously monitoring heart rate variability in the  
4 premature newborn infant; and  
5 (b) a microprocessor, identifying at least one characteristic abnormality in the heart  
6 rate variability that is associated with the illness.

1 29. The apparatus of claim 28, wherein the microprocessor performs the step of  
2 generating a normalized data set of RR intervals.

1 30. The apparatus of claim 29, wherein the microprocessor calculates one or more  
2 of the third and higher moments of the data set and identifies the characteristic  
3 abnormality based on the one or more moments.

1 31. The apparatus of claim 30, wherein the microprocessor calculates the skewness  
2 of the data set and identifies the characteristic abnormality based on the skewness.

1 32. The apparatus of claim 30, wherein the microprocessor calculates the kurtosis of  
2 the data set and identifies the characteristic abnormality based on the kurtosis.

1 33. The apparatus of claim 29, wherein the microprocessor calculates one or more  
2 percentile values of the data set and identifies the characteristic abnormality based  
3 on the one or more percentile values.

1 34. The apparatus of claim 33, wherein the microprocessor calculates the 10th  
2 percentile value of the data set and identifies the characteristic abnormality based on  
3 the 10th percentile value.

1 35. An apparatus for early detection of subacute, potentially catastrophic infectious  
2 illness in a patient comprising (1) a monitoring device, continuously monitoring the  
3 patient's RR intervals, and (2) a microprocessor, said microprocessor performing  
4 steps comprising:  
5 (a) generating a normalized data set of the RR intervals;

- 6 (b) calculating one or more of (i) moments of the data set selected from the  
7 third and higher moments and (ii) percentile values of the data set;  
8 (c) identifying an abnormal heart rate variability based on one or more of  
9 the moments and the percentile values.

1 36. The apparatus of claim 35, wherein the microprocessor calculates the third  
2 moment of the data set.

1 37. The apparatus of claim 35, wherein the microprocessor calculates the fourth  
2 moment of the data set.

1 38. The apparatus of claim 35, wherein the microprocessor calculates the 10th  
2 percentile of the data set.